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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,129	06/19/2003	Sarah S. Bacus	02-434-A	9778

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/28/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/600,129	BACUS ET AL.	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *1-28 and 35-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/06 and 8/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group IV (claims 29-34) in the reply filed on 10/11/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-38 are pending. Claims 1-28 and 35-38, drawn to non-elected inventions, are withdrawn from consideration.

Claims 29-34 are examined on the merits.

Claim Rejections - 35 USC § 112

2. Claims 29-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29-32 are indefinite because claim 29 is drawn to a method comprising the step of treating a subject with an anti-EGFR antibody when HER3 expression levels in the cell are low. There is no definition in the specification for what is meant by "low" expression levels of HER3. What is the cut-off?

Claims 29-34 are indefinite because claim 29 is drawn to a method comprising the step of determining expression of HER3 in cells from a subject instead of determining levels of HER3 in cells from the cancer.

3. Claims 30, 32 and 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not set forth in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 30, 32 and 34 are drawn to methods using the ABX-0303 monoclonal antibody. The specification fails to describe how to make the ABX-0303 monoclonal antibody, except to refer to US Patent 6,235,883, and indicates that ABX-0303 is the antibody produced by hybridoma E7.6.3. However, US Patent 6,235,883 does not refer to hybridoma E7.6.3. Therefore, the reference to US Patent 6,235,883 does not appear to be sufficient disclosure for how to make ABX-0303. Furthermore, the specification fails to provide enough information for one of skill in the art to produce a monoclonal antibody with exactly the same characteristics as the ABX-0303 monoclonal antibody. Even if the specification did provide enough information for one of skill in the art to produce a monoclonal antibody with properties similar to those of the ABX-0303 monoclonal antibody, reproduction of an identical monoclonal antibody is an unpredictable event. Because it does not appear that the ABX-0303 monoclonal antibody is publicly available or can be reproducibly isolated from nature without undue experimentation, one of ordinary skill in the art cannot be assured of the ability to practice the claimed inventions. Because claims 30, 32 and 34 specifically require the use of the ABX-0303 monoclonal antibody, a suitable deposit of the hybridoma producing the ABX-0303 monoclonal antibody is required, or evidence must be provided that the ABX-0303 monoclonal antibody is well known and readily available to the public, or that it is reproducible without undue experimentation.

Furthermore, unless a deposit was made at or before the time of filing, a declaration filed under the 37 C.F.R. 1.132 is necessary to construct a chain of custody. The declaration, executed by a person in a position to know, should identify the deposited hybridoma by its depository accession number, establish that the deposited hybridoma is the same as that described in the specification, and establish that the deposited hybridoma was in applicant's possession at the time of filing. Applicant is required to amend the specification to recite the accession number of the deposit, the date of deposit, a description of the deposited biological material, and the name and address of the depository. See In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

If the deposit is made under the provision of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the Budapest Treaty as the treaty leaves this specific matter to the discretion of each member state.

If the deposits are not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an

attorney of record who has the authority and control over the conditions of deposit, over his or her signature and registration number, averring:

(a) that all restrictions on the availability to the public of the material will be irrevocably removed upon the granting of a patent.

(b) that the material has been deposited under conditions that ensure that access to the material will be available during the pendancy of the patent application to one determined by the Commissioner to be entitled thereto under 35 CFR 1.14 and 35 USC 122.

(c) that the deposited material will be stored with all care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case at least thirty (30) years after the date of a deposit or for the enforceable life of the patent, whichever is longer.

(d) that the duty to replace the deposit should the depository be unable to furnish a sample when requested due to the condition of the deposit.

4. Claims 29-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating a subject with cancer that expresses EGFR, does not reasonably provide enablement for treating a subject with any type of cancer regardless of the EGFR status of the cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation

necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The claims are broadly drawn to treatment of a subject with cancer, without any limitation on the type of cancer. The active steps recited in the claims are first to determine levels of HER3 in the cancer of the subject and then to administer an anti-EGFR antibody to the subject with cancer if the HER3 expression levels are low. Therefore, the claims read on administering an anti-EGFR antibody to a subject regardless of the EGFR status of the cancer. It is quite clear from the prior art that EGFR-targeted therapies require that the cancer express some level of EGFR (see Baselga, J. The Oncologist, 7(suppl 4): 2-8, 2002). Additionally the working examples provided in the specification are narrowly confined to demonstrating that HER1 (EGFR) and pERK expression levels are correlated with a response to ABX-0303, whereas expression of HER3 is negatively correlated with response to ABX-0303.

Therefore, in view of the teachings of the specification in combination with that of the prior art, one of skill in the art would have to engage in further experimentation to discover methods using anti-EGFR antibodies useful for treating any and all cancers. Therefore, the full scope of the claimed methods are not enabled by the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 29, 31 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herbst (Herbst, R.S. et al., Expert Opin. Biol. Ther., 1(4): 719-732, 2001) in view of Xia (Xia, W. et al. Clinical Cancer Res. 5: 4164-4174, 1999).

Claims 29 and 33 are drawn to a method for treating a subject with cancer comprising determining the level of expression of HER3 in cells from the subject and treating the subject with an anti-EGFR antibody when HER3 expression levels in the cell are low or undetectable. Claim 31 is drawn to a method of further measuring one or more of HER1(EGFR), pHER1, HER2/neu and pERK.

Xia teaches methods comprising determining levels of expression of EGFR, HER3 and HER2, and teaches that cancers such as oral squamous cell carcinomas (SCC) express HER3, whereas head and neck SCC do not tend to express HER3, and that in oral SCC HER3 is useful prognostic indicator, whereas in head and neck SCC, HER3 is not a useful prognostic indicator (see page 4169-4170, bridging paragraph), and that expression of EGFR is characteristic of SCC of head and neck. Xia fails to teach treating cancers with low HER3 with an anti-EGFR

antibody. However, Herbst teaches methods of targeting the EGFR in head and neck SCC, because in head and neck SCC, Her1 levels are high. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have measured levels of HER1 and then used an anti-EGFR antibody to treat a cancer such as head and neck SCC, which is a cancer that expresses low levels of HER3 and instead expresses high levels of EGFR, because Herbst teaches that EGFR blockade using anti-EGFR antibodies is a promising target for SCC of the head and neck.

6. Claims 29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herbst (Herbst, R.S. et al., Expert Opin. Biol. Ther., 1(4): 719-732, 2001) in view of Xia (Xia, W. et al. Clinical Cancer Res. 5: 4164-4174, 1999) and further in view of Yang (Yang, X.-D. et al., Critical Reviews in Oncology/Hematology, 38: 17-23, 2001).

Claims 30, 32 and 34 are drawn to methods using an the ABX-0303 antibody (which the specification teaches is also known as ABX-EGF)

The combination of Herbst and Xia teach as set forth above for claims 29, 31 and 33. Neither Herbst or Xia teaches methods comprising the use of ABX-0303. However, ABX-0303 appears to be a useful anti-EGFR antibody, because Yang teaches that it is a completely human antibody, and because it completely eradicates a human tumor xenograft (see page 20, section 2.3). Also, Yang teaches that the antibody appears to be useful in xenografts that express high levels of EGFR. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used Yang's ABX-EGF antibody instead of the antibody of Herbst (C225) for the treatment of SCC of head and neck, a cancer that expresses

low levels of HER3. One would have been motivated by the teachings of Yang with regard to efficacy of the ABX-EGF antibody and also because the ABX-EGF antibody is a fully human antibody which lessen the immune response that a human subject would have to the administration of an antibody.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
December 20, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER